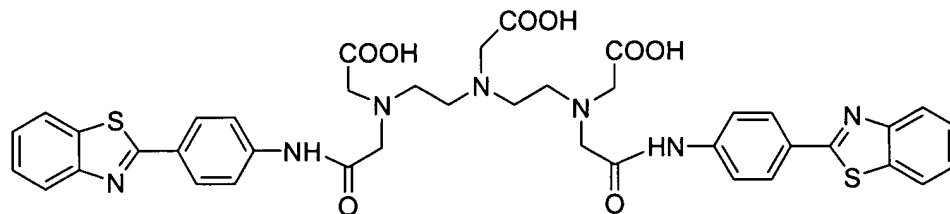


## Claims

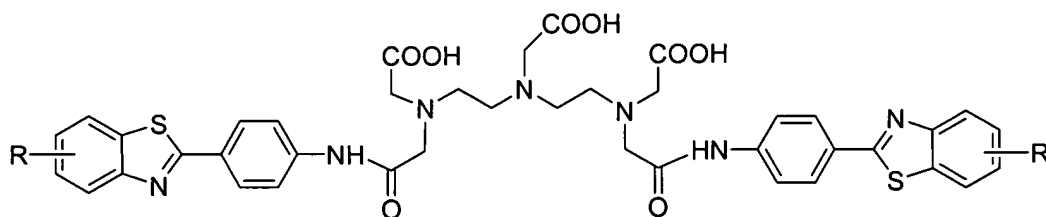
What is claimed is:

1. A bifunctional molecule comprising at least one metal-chelating moiety associated with at least one amyloid-binding moiety.
2. The bifunctional molecule of claim 1, wherein the metal-chelating moiety binds with high affinity at least one transition metal ion selected from the group consisting of zinc II ( $\text{Zn}^{2+}$ ), copper II ( $\text{Cu}^{2+}$ ), and iron III ( $\text{Fe}^{3+}$ ).
3. The bifunctional molecule of claim 1, wherein the metal-chelating moiety comprises DTPA.
4. The bifunctional molecule of claim 1, wherein the metal-chelating moiety comprises an  $\alpha$ -lipoic acid derivative.
5. The bifunctional molecule of claim 1, wherein the amyloid-binding moiety is blood-brain barrier permeable.
6. The bifunctional molecule of claim 1, wherein the amyloid-binding moiety has a high affinity and specificity for A $\beta$  amyloid deposits.
7. The bifunctional molecule of claim 1, wherein the amyloid-binding moiety comprises a benzothiazole derivative.
8. The bifunctional molecule of claim 1, wherein the metal-chelating moiety binds with high affinity at least one transition metal ion selected from the group consisting of zinc II ( $\text{Zn}^{2+}$ ), copper II ( $\text{Cu}^{2+}$ ), and iron III ( $\text{Fe}^{3+}$ ), and wherein the amyloid-binding moiety has a high affinity and specificity for A $\beta$  amyloid deposits.
9. The bifunctional molecule of claim 8, wherein the metal-chelating moiety comprises DTPA.

10. The bifunctional molecule of claim 8, wherein the amyloid-binding moiety comprises a benzothiazole derivative.
11. The bifunctional molecule of claim 8, wherein the metal-chelating moiety comprises DTPA, and wherein the amyloid-binding moiety comprises a benzothiazole derivative.
12. A bifunctional molecule with the following chemical structure:

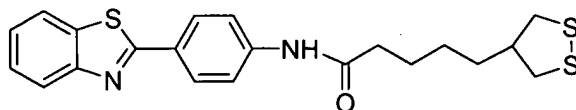


13. A bifunctional molecule with the following chemical structure:

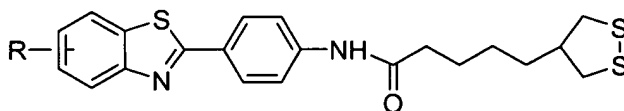


wherein R is selected from the group consisting of 4-dimethylamino, 4-amino, 4-chloro, 4-chloro-5-ethyl, 4-acetyl, 5-carboxyl, 5-sulfonyl, 5-bromo, 4-methyl, 5-methyl, 6-methyl, 5-trifluoromethyl, 4-ethoxyl, 4-methylsulfonyl, 5-methylsulfonyl, 6-methylsulfonyl, 4-hydroxyl, 5-hydroxyl, and 6-hydroxyl.

14. A bifunctional molecule with the following chemical structure:



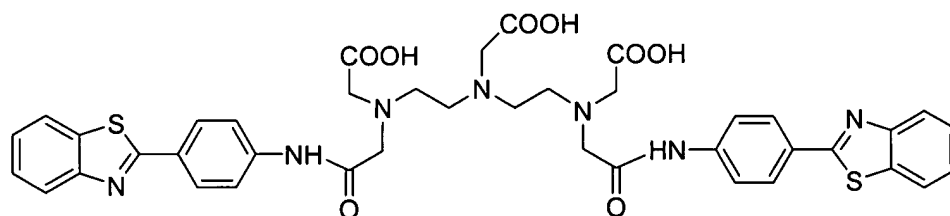
15. A bifunctional molecule with the following chemical structure:



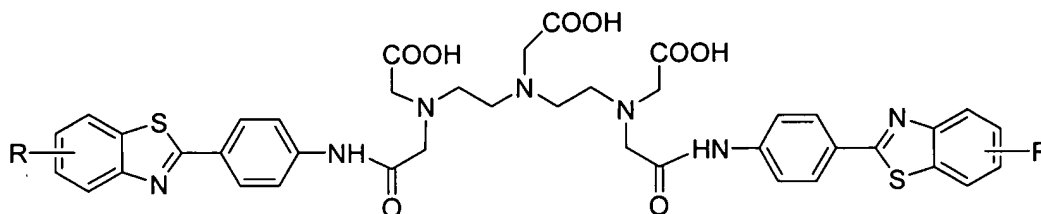
wherein R is selected from the group consisting of 4-dimethylamino, 4-amino, 4-chloro, 4-chloro-5-ethyl, 4-acetyl, 5-carboxyl, 5-sulfonyl, 5-bromo, 4-methyl, 5-methyl, 6-methyl, 5-trifluoromethyl, 4-ethoxyl, 4-methylsulfonyl, 5-methylsulfonyl, 6-methylsulfonyl, 4-hydroxyl, 5-hydroxyl, and 6-hydroxyl.

16. A contrast imaging agent comprising at least one imaging moiety associated with at least one amyloid-binding moiety.
17. The contrast imaging agent of claim 16, wherein the amyloid-binding moiety is blood-brain barrier permeable.
18. The contrast imaging agent of claim 16, wherein the amyloid-binding moiety has a high affinity and specificity for A $\beta$  amyloid deposits.
19. The contrast imaging agent of claim 16, wherein the amyloid-binding moiety comprises a benzothiazole derivative.
20. The contrast imaging agent of claim 16, wherein the imaging moiety comprises at least one metal-chelating moiety complexed to a metal entity.
21. The contrast imaging agent of claim 20, wherein the metal-chelating moiety comprises DTPA.
22. The contrast imaging agent of claim 16, wherein the imaging moiety comprises at least one metal-chelating moiety complexed to a metal entity, and wherein the amyloid-binding moiety has a high affinity and specificity for A $\beta$  amyloid deposits.
23. The contrast imaging agent of claim 22, wherein the metal-chelating moiety comprises DTPA, and wherein the amyloid-binding moiety comprises a benzothiazole derivative.
24. The contrast imaging agent of claim 20 or 22, wherein the metal entity is a paramagnetic metal ion.

25. The contrast imaging agent of claim 20 or 22, wherein the metal entity is a paramagnetic metal ion selected from the group consisting of gadolinium III ( $Gd^{3+}$ ), chromium III ( $Cr^{3+}$ ), dysprosium III ( $Dy^{3+}$ ), iron III ( $Fe^{3+}$ ), manganese II ( $Mn^{2+}$ ), and ytterbium III ( $Yb^{3+}$ ).
26. The contrast imaging agent of claim 20 or 22, wherein the metal entity is gadolinium III ( $Gd^{3+}$ ).
27. The contrast imaging agent of claim 20 or 22, wherein the metal entity is a radionuclide.
28. The contrast agent of claim 20 or 22, wherein the metal entity is a radionuclide selected from the group consisting of technetium-99m ( $^{99m}Tc$ ), gallium-67 ( $^{67}Ga$ ), yttrium-91 ( $^{90}Y$ ), indium-111 ( $^{111}In$ ), rhenium-186 ( $^{186}Re$ ), and thallium-201 ( $^{201}Tl$ ).
29. The contrast imaging agent of claim 20 or 22, wherein the metal entity is technetium-99m ( $^{99m}Tc$ ).
30. A contrast imaging agent, wherein gadolinium III ( $Gd^{3+}$ ) is complexed to a bifunctional molecule with the following chemical structure:



31. A contrast imaging agent, wherein gadolinium III ( $Gd^{3+}$ ) is complexed to a bifunctional molecule with the following chemical structure:



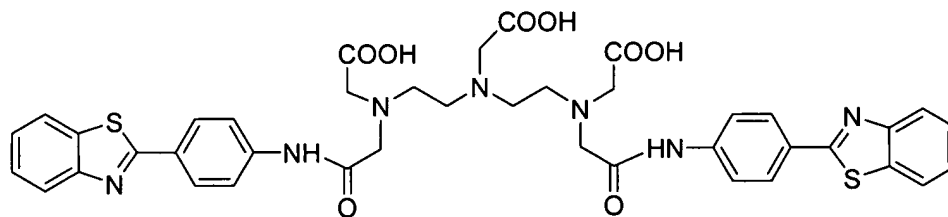
wherein R is selected from the group consisting of 4-dimethylamino, 4-amino, 4-chloro, 4-chloro-5-ethyl, 4-acetyl, 5-carboxyl, 5-sulfonyl, 5-bromo, 4-methyl, 5-methyl,

6-methyl, 5-trifluoromethyl, 4-ethoxyl, 4-methylsulfonyl, 5-methylsulfonyl, 6-methylsulfonyl, 4-hydroxyl, 5-hydroxyl, and 6-hydroxyl.

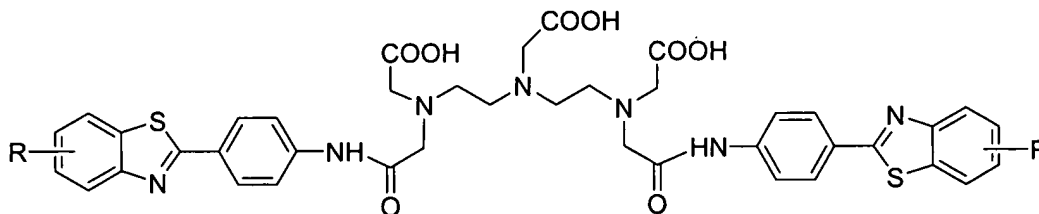
32. A contrast imaging agent comprising at least one metal-chelating moiety associated with at least one amyloid-binding moiety labeled with a stable paramagnetic isotope.
33. The contrast imaging agent of claim 32, wherein the stable paramagnetic isotope is carbone-13 ( $^{13}\text{C}$ ) or fluorine-19 ( $^{19}\text{F}$ ).
34. A pharmaceutical composition comprising an effective amount of at least one bifunctional molecule of claim 1, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
35. A pharmaceutical composition comprising an effective amount of at least one bifunctional molecule of claim 8, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
36. A pharmaceutical composition comprising an effective amount of at least one bifunctional molecule of claim 12, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
37. A pharmaceutical composition comprising an effective amount of at least one bifunctional molecule of claim 13, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
38. A pharmaceutical composition comprising an effective amount of at least one bifunctional molecule of claim 14, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
39. A pharmaceutical composition comprising an effective amount of at least one bifunctional molecule of claim 15, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.

40. A pharmaceutical composition comprising an imaging effective amount of at least one contrast imaging agent of claim 16, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
41. A pharmaceutical composition comprising an imaging effective amount of at least one contrast imaging agent of claim 20, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
42. A pharmaceutical composition comprising an imaging effective amount of at least one contrast imaging agent of claim 25, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
43. A pharmaceutical composition comprising an imaging effective amount of the contrast imaging agent of claim 28, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
44. A pharmaceutical composition comprising an imaging effective amount of the contrast imaging agent of claim 30, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
45. A pharmaceutical composition comprising an imaging effective amount of at least one contrast imaging agent of claim 31, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.
46. A method for reducing or inhibiting amyloid toxicity in a system, comprising contacting the system with a bifunctional molecule of claim 1, or a pharmaceutical composition thereof.
47. The method of claim 46, wherein said method prevents, slows down or stops amyloid accumulation in the system; or promotes, induces, or otherwise facilitates dissolution of amyloid deposits present in the system; or both.

48. The method of claim 46, wherein said method reduces, inhibits or otherwise interferes with amyloid-mediated production of reactive oxygen species.
49. The method of claim 46, wherein the contacting is carried out by *in vitro* or *ex vivo* incubation, and wherein the system is selected from the group consisting of a cell, a biological fluid, and a biological tissue.
50. The method of claim 49, wherein the cell, biological fluid, or biological tissue originates from a patient suspected of having a pathophysiological condition associated with amyloid accumulation.
51. The method of claim 50, wherein the pathophysiological condition is associated with accumulation of the amyloid- $\beta$  peptide, and wherein the amyloid-binding moiety in the bifunctional molecule has a high affinity and specificity for A $\beta$  amyloid deposits.
52. The method of claim 46, wherein the bifunctional molecule has the following chemical structure:

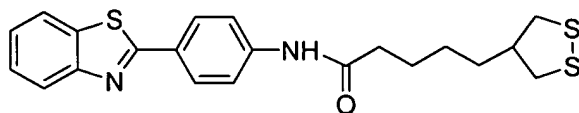


53. The method of claim 46, wherein the bifunctional molecule has the following chemical structure:

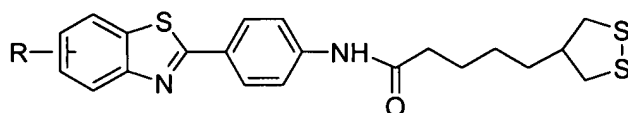


wherein R is selected from the group consisting of 4-dimethylamino, 4-amino, 4-chloro, 4-chloro-5-ethyl, 4-acetyl, 5-carboxyl, 5-sulfonyl, 5-bromo, 4-methyl, 5-methyl, 6-methyl, 5-trifluoromethyl, 4-ethoxyl, 4-methylsulfonyl, 5-methylsulfonyl, 6-methylsulfonyl, 4-hydroxyl, 5-hydroxyl, and 6-hydroxyl.

54. The method of claim 46, wherein the bifunctional molecule has the following chemical structure:



55. The method of claim 46, wherein the bifunctional molecule has the following chemical structure:

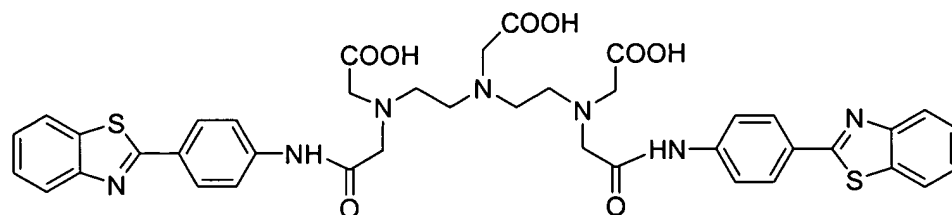


- wherein R is selected from the group consisting of 4-dimethylamino, 4-amino, 4-chloro, 4-chloro-5-ethyl, 4-acetyl, 5-carboxyl, 5-sulfonyl, 5-bromo, 4-methyl, 5-methyl, 6-methyl, 5-trifluoromethyl, 4-ethoxyl, 4-methylsulfonyl, 5-methylsulfonyl, 6-methylsulfonyl, 4-hydroxyl, 5-hydroxyl, and 6-hydroxyl.
56. A method for treating a patient with a pathophysiological condition associated with amyloid accumulation, comprising administering to the patient an effective amount of a bifunctional molecule of claim 1, or a pharmaceutical composition thereof.
57. The method of claim 56, wherein said method prevents, slows down, or stops amyloid accumulation in the patient; or promotes, induces, or otherwise facilitates dissolution of amyloid deposits present in the patient; or both.
58. The method of claim 56, wherein said method reduces, inhibits or otherwise interferes with amyloid-mediated production of reactive oxygen species.
59. The method of claim 56, wherein the administration is carried out by a method selected from the group consisting of oral and parenteral administrations, including intravenous, intramuscular, subcutaneous injections, and transdermal and enteral administrations.

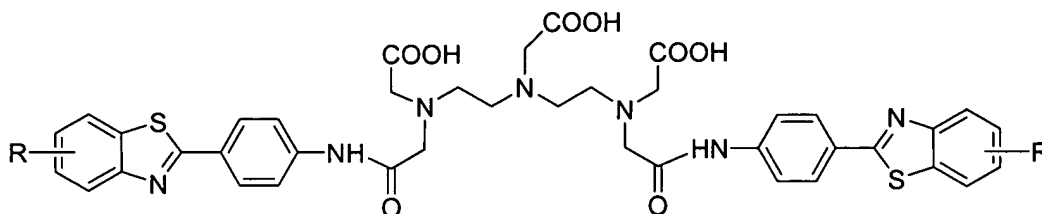


60. The method of claim 56, wherein the pathophysiological condition is associated with accumulation of the amyloid- $\beta$  peptide, and wherein the amyloid-binding moiety in the bifunctional molecule has a high affinity and specificity for A $\beta$  amyloid deposits.

61. The method of claim 56, wherein the bifunctional molecule has the following chemical structure:

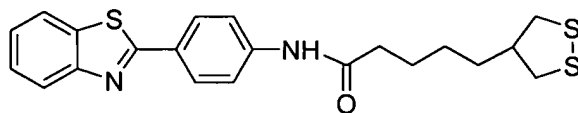


62. The method of claim 56, wherein the bifunctional molecule has the following chemical structure:

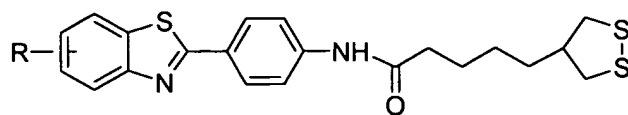


wherein R is selected from the group consisting of 4-dimethylamino, 4-amino, 4-chloro, 4-chloro-5-ethyl, 4-acetyl, 5-carboxyl, 5-sulfonyl, 5-bromo, 4-methyl, 5-methyl, 6-methyl, 5-trifluoromethyl, 4-ethoxyl, 4-methylsulfonyl, 5-methylsulfonyl, 6-methylsulfonyl, 4-hydroxyl, 5-hydroxyl, and 6-hydroxyl.

63. The method of claim 56, wherein the bifunctional molecule has the following chemical structure:



64. The method of claim 56, wherein the bifunctional molecule has the following chemical structure:



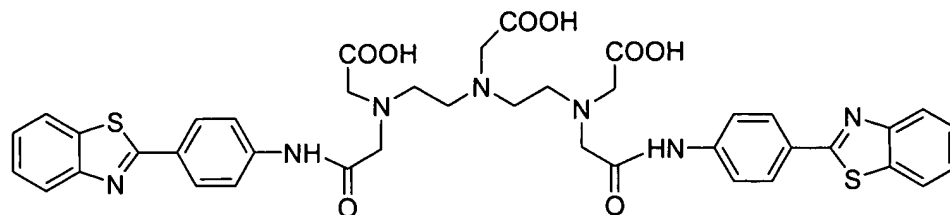
wherein R is selected from the group consisting of 4-dimethylamino, 4-amino, 4-chloro, 4-chloro-5-ethyl, 4-acetyl, 5-carboxyl, 5-sulfonyl, 5-bromo, 4-methyl, 5-methyl, 6-methyl, 5-trifluoromethyl, 4-ethoxyl, 4-methylsulfonyl, 5-methylsulfonyl, 6-methylsulfonyl, 4-hydroxyl, 5-hydroxyl, and 6-hydroxyl.

65. The method of claim 56, wherein the pathophysiological condition is selected from the group consisting of Alzheimer's disease, Down's syndrome, Lewy body dementia, hereditary cerebral hemorrhage with amyloidosis (Dutch type), Guam Parkinson-Dementia, and head trauma.
66. The method of claim 56, wherein the pathophysiological condition is Alzheimer's disease.
67. A method for detecting the presence of amyloid deposits in a system comprising steps of:  
 contacting the system with an imaging effective amount of a contrast imaging agent of claim 20, or a pharmaceutical composition thereof, under conditions to allow the contrast imaging agent to interact with any amyloid deposit present so that the interaction results in binding of the contrast imaging agent to the amyloid deposit;  
 detecting any amyloid deposit present in the system and bound to the contrast imaging agent, using an imaging technique; and  
 generating one or more images of at least part of the system.
68. The method of claim 67, wherein the amyloid deposits present in the system are formed by accumulation of the amyloid- $\beta$  peptide, and wherein the amyloid-binding moiety in the contrast imaging agent has a high affinity for A $\beta$  amyloid deposits.
69. The method of claim 67, wherein the contacting is carried out by *in vitro* or *ex vivo* incubation, and wherein the system is selected from the group consisting of a cell, a biological fluid, and a biological tissue.

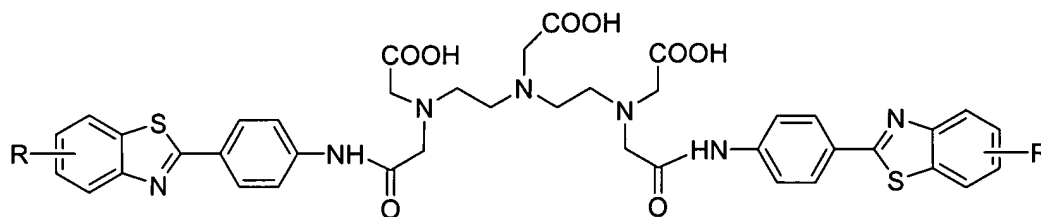
70. The method of claim 69, wherein the cell, biological fluid, or biological tissue originates from a patient suspected of having a pathophysiological condition associated with amyloid accumulation.
71. The method of claim 69, wherein the cell, biological fluid, or biological tissue originates from a patient receiving a treatment for a pathophysiological condition associated with amyloid accumulation.
72. The method of claim 69, wherein the cell, biological fluid, or biological tissue has been contacted with a potential therapeutic agent for the treatment of a pathophysiological condition associated with amyloid accumulation.
73. The method of claim 67, wherein said method is used to identify potential therapeutic agents for the treatment of a pathophysiological condition associated with amyloid accumulation.
74. The method of claim 67, wherein said method is used to diagnose a pathophysiological condition associated with amyloid accumulation.
75. The method of claim 67, wherein said method is used to follow the progression of a pathophysiological condition associated with amyloid accumulation.
76. The method of claim 67, wherein said method is used to monitor the response of a patient to a treatment for a pathophysiological condition associated with amyloid accumulation.
77. A method for detecting the presence of amyloid deposits in a patient comprising steps of:
  - administering to the patient an imaging effective amount of a contrast imaging agent of claim 20, or a pharmaceutical composition thereof, under conditions to allow the contrast imaging agent to interact with any amyloid deposit present so that the interaction results in binding of the contrast imaging agent to the amyloid deposit;
  - detecting any amyloid deposit present in the patient and bound to the contrast imaging agent, using an imaging technique; and
  - generating one or more images of at least part of the body of the patient.

78. The method of claim 77, wherein the administration is carried out by a method selected from the group consisting of oral and parenteral administrations, including intravenous, intraarterial, intrathecal, intradermal, and intracavitary administrations, and enteral administration.
79. The method of claim 77, wherein the amyloid deposits are formed by aggregation and accumulation of the amyloid- $\beta$  peptide, and wherein the amyloid-binding moiety in the contrast imaging agent has a high affinity or specificity for A $\beta$  amyloid deposits.
80. The method of claim 77, wherein said method is used to localize amyloid deposits in a patient.
81. The method of claim 77, wherein said method is used to localize amyloid deposits in the brain of a patient; and wherein the amyloid-binding moiety in the contrast imaging agent is blood-brain barrier permeable.
82. The method of claim 77, wherein said method is used to diagnose a pathophysiological condition associated with amyloid accumulation.
83. The method of claim 77, wherein said method is used to follow the progression of a pathophysiological condition associated with amyloid accumulation.
84. The method of claim 77, wherein said method is used to monitor the response of a patient to a treatment for a pathophysiological condition associated with amyloid accumulation.
85. The method of claim 67 or 77, wherein the imaging moiety in the contrast imaging agent comprises at least one metal-chelating moiety complexed to a paramagnetic metal ion; the detection is carried out by Magnetic Resonance Imaging (MRI); and MR images are generated.
86. The method of claim 85, wherein the paramagnetic metal ion is selected from the group consisting of gadolinium III (Gd<sup>3+</sup>), chromium III (Cr<sup>3+</sup>), dysprosium III (Dy<sup>3+</sup>), iron III (Fe<sup>3+</sup>), manganese II (Mn<sup>2+</sup>), and ytterbium III (Yb<sup>3+</sup>).
87. The method of claim 85, wherein the paramagnetic metal ion is gadolinium III (Gd<sup>3+</sup>).

88. The method of claim 87, wherein gadolinium III ( $Gd^{3+}$ ) is complexed to a bifunctional molecule with the following chemical structure:



89. The method of claim 87, wherein gadolinium III ( $Gd^{3+}$ ) is complexed to a bifunctional molecule with the following chemical structure:



wherein R is selected from the group consisting of 4-dimethylamino, 4-amino, 4-chloro, 4-chloro-5-ethyl, 4-acetyl, 5-carboxyl, 5-sulfonyl, 5-bromo, 4-methyl, 5-methyl, 6-methyl, 5-trifluoromethyl, 4-ethoxyl, 4-methylsulfonyl, 5-methylsulfonyl, 6-methylsulfonyl, 4-hydroxyl, 5-hydroxyl, and 6-hydroxyl.

90. The method of claim 67 or 77, wherein the imaging moiety in the contrast imaging agent comprises at least one metal-chelating moiety complexed to a radionuclide; the detection is carried out by Single Photon Emission Computed Tomography (SPECT); and SPECT images are generated.
91. The method of claim 90, wherein the radionuclide is selected from the group consisting of technetium-99m ( $^{99m}Tc$ ), gallium-67 ( $^{67}Ga$ ), yttrium-91 ( $^{90}Y$ ), indium-111 ( $^{111}In$ ), rhenium-186 ( $^{186}Re$ ), and thallium-201 ( $^{201}Tl$ ).
92. The method of claim 90, wherein the radionuclide is technetium-99m ( $^{99m}Tc$ ).
93. The method of claim 73, 74, 75, 76, 82, 83 or 84, wherein the pathophysiological condition is associated with accumulation of the amyloid- $\beta$  peptide, and wherein the

amyloid-binding moiety in the contrast imaging agent has a high affinity for A $\beta$  amyloid deposits.

94. The method of claim 73, 74, 75, 76, 82, 83 or 84, wherein the pathophysiological condition is selected from the group consisting of Alzheimer's disease, Down's syndrome, Lewy body dementia, hereditary cerebral hemorrhage with amyloidosis (Dutch type), Guam Parkinson-Dementia, and head trauma.
95. The method of claim 73, 74, 75, 76, 82, 83 or 84, wherein the pathophysiological condition is Alzheimer's disease.